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Atrial fibrillation in athletes and general population

A systematic review and meta-analysis

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Abstract

Background: Atrial fibrillation (AF) is the most common type of heart arrhythmia, but the impact of long-term, high-intensity endurance exercise on the risk of AF remains uncertain.

Methods: PubMed, EMBASE, and Cochrane library databases were searched till Nov 2017 to retrieve the articles. The included studies were summarized, pooled odds ratio (OR) and its 95% confidence interval (CI) were calculated. Both fixed and random effects models were used to combine the data. Stratified and logistic meta-regression analyses were performed to explore the sources of heterogeneity across studies.

Results: Nine studies including 2308 athletes and 6593 controls were eligible. Our results showed that the risk of AF was significantly higher in athletes than in general population (OR=2.34, 95% CI=1.04–5.28, $P_{heterogeneity}<.001$, $I^2=92.3\%$). Subgroup analysis based on gender and mean age demonstrated a significantly increased risk in men (OR=4.03, 95% CI=1.73–9.42, $P_{heterogeneity}<.001$, $I^2=82.7\%$) and participants with mean age <60 (OR=3.24, 95% CI=1.23–8.55, $P_{heterogeneity}<.001$, $I^2=84.3\%$). Furthermore, subgroup analysis based on type of athletes demonstrated a significantly increased risk of AF in participants with single type of sport (OR=3.97, 95% CI=1.16–13.62, $P_{heterogeneity}=.018$, $I^2=70.4\%$). Results remained unchanged after performing sensitivity analysis. Meta-regression showed that gender, age, type of study, sample size, and sports mode were unrelated to heterogeneity.

Conclusion: Our study confirmed that the risk of AF was significantly higher in athletes than in general population, especially among men and participants aged <60.

Abbreviations: AF = atrial fibrillation, CI = confidence interval, OR = odds ratio, STROBE = Strengthening the Reporting of Observational Studies in Epidemiology.

Keywords: athletes, atrial fibrillation, general population, meta-analysis, systematic review

1. Introduction

Atrial fibrillation (AF) is the most commonly encountered type of heart arrhythmia in clinical practice, and its prevalence increases with advancing age.[1,2] In general population, the average prevalence of AF was 0.5% in subjects aged 45 to 54 years, about 1% in 54 to 64 years, and 4% in 65 to 74 years.[2] The Framingham Heart Study and other studies have identified male sex, advancing age, diabetes mellitus, hypertension, heart failure, obesity, myocardial infarction (MI), valve disease, and alcohol consumption as main risk factors for AF.[3–6]

Growing evidence strongly supports the cardiac risk factor modification, which includes increasing cardio-pulmonary fitness (such as traditional modifiable cardiac risk factors, weight loss, and exercise) for the management of AF.[7–10] It was speculated that long-term endurance exercise practice may promote changes in the cardiac structure, increase vagal tone, bradycardia, inducing AF.[11–14] The grading benefits of exercise on cardiovascular health and mortality have been demonstrated in several observational and cohort studies.[15–18] However, there is considerable uncertainty about the impact of long-term, high-intensity endurance exercise on the risk of AF. Therefore, we conducted this systematic review and meta-analysis to quantitatively assess the risk of AF in athletes and general population.

2. Materials and methods

The present meta-analysis was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-analysis(PRISMA) guidelines.[19]

2.1. Search Strategy

An extensive searching through PubMed, Embase, Cochrane Library Databases (most recently updated in 2017 November),

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using the search terms "AF", "athletes", and "endurance exercise" was done. Two reviewers independently performed the search and any disagreements regarding the eligibility were resolved through discussion. There were no search limitations concerning publication language and study design but limited to observational studies. We tried to identify potentially relevant studies from the whole reference lists by orderly reviewing title, abstract and full text.

2.2. Selection criteria

The inclusion criteria were as follows:

1. Case-control or cohort studies that focused on the association of endurance exercise and AF;
2. Comparison of athletes group with non-athletes group (control).

Studies were excluded for the following reasons:

1. unpublished papers, reviews, and duplication of publications;
2. data unavailable for AF;
3. no control population. If more than 1 article was published using the same case series, we selected the study with the largest sample size.

2.3. Data extraction and quality assessment

All the available data were extracted from each study by 2 investigators independently according to the inclusion criteria listed above. For each study, we recorded the first author, year of publication, country of origin, gender, mean age, study design, sports mode, follow-up time, the number of cases and controls, and outcomes. Any disagreement was resolved by discussing with the third expert. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) recommendations were followed on the methodological evaluation of what should be included in an accurate and complete report of observational studies.[20] The STROBE statement is a checklist of 22 items that are essential for good reporting of observational studies (Table 2). These items relate to the article's title and abstract (item 1), the introduction (items 2 and 3), methods (items 4–12), results (items 13–17), discussion sections (items 18–21), and other information (item 22 on funding).

2.4. Statistical analysis

The pooled odds ratio (OR) with corresponding 95% confidence interval (CI) was estimated. Heterogeneity of the studies was assessed using the Cochran Q test and was quantified by I^2 statistic (considered high heterogeneity for $I^2 > 50\%$).[21] Preliminary analysis was performed using a fixed effects model (Mantel–Haenszel method) and using a random effects model (Der Simonian and Laird) if there is high heterogeneity.[22] To explore the sources of heterogeneity across studies, we did stratified and logistic meta-regression analyses. Relative influence of each study on the pooled estimate was assessed by omitting 1 study at a time for sensitivity analysis. Publication bias was evaluated by visual inspection of symmetry of funnel plot and assessment of Begg and Egger test.[23] Statistical analyses were done using STATA software, version 12.0 (STATA Corp., College Station, TX). $P < .05$ were considered as representative of statistical significance and all tests were 2-sided.

Table 1

Characteristics of the studies included in this meta-analysis.

Authors/year of publication	Country	Male (%)	Mean age	Study design	Sports mode	Follow-up time	Atrial fibrillation/ athletes (N)	Atrial fibrillation/ general population (N)	Outcomes
Karjalainen/1998	Finland	100	Athletes: 47.5±7.0Y; Control: 49.6±5.3Y	Case-control	Top-level orienteers (runners)	NA	12/228	2/212	Prevalence of AF
Elosua/2006	Spain	100	43.2±11.9Y	Case-control	Mixed, mainly aerobic cyclist	NA	16/31	35/129	Prevalence of AF
Heidbuchel/2006	Belgium	83	Athletes: 53±9.0Y; Control: 60±10Y	Cohort	Mixed sports	2.5Y	25/31	51/106	Prevalence of AF
Baldesberger/2008	Switzerland	100	Athletes: 66±6Y; Control: 66±7Y	Case-control	Former Swiss elite cyclists	30–50Y	6/62	0/62	Prevalence of AF
Molina/2008	Spain	100	Athletes: 39±9Y; Control: 50±13Y	Cohort	Marathon runners	11.6Y	9/183	2/290	Prevalence of AF
Mont/2008	Spain	100	47.8±10.9Y	Case-control	Mixed sports	NA	83/120	24/96	Prevalence of AF
Mozaffarian /2008	USA	42	72.8±5.6Y	Cohort	Mixed sports	12Y	65/505	127/477	Prevalence of AF
Myrstad/2014	Norway	100	Athletes: 68.9Y; Control: 71.6Y	Cross-sectional study	Cross-country ski racing	NA	66/509	183/1867	Prevalence of AF
Sun/2015	China	46	53.8Y	Cross-sectional study	Mixed sports	NA	6/639	75/3354	Prevalence of AF

AF=atrial fibrillation, NA=not available, USA=United States of America, Y=years.

Table 2

Methodological quality of included studies (STROBE criteria).

	Authors & Year								
Variables	Karjalainen/ 1998	Elosua/ 2006	Heidbchel/ 2006	Baldesberger /2008	Molina/ 2008	Mont/ 2008	Mozaffarian/ 2008	Myrstad/ 2014	Sun/ 2015
Title/abstract	☆	☆	☆	☆	☆	☆	☆	☆	☆
Introduction									
Background/rationale	☆	☆	☆	☆	☆	☆	☆	☆	☆
Objectives	☆	☆	☆	☆	☆	☆	☆	☆	☆
Methods									
Study design		☆	☆	☆	☆	☆	☆	☆	
Setting	☆	☆	☆	☆	☆	☆	☆	☆	☆
Participants	☆	☆	☆	☆	☆	☆	☆	☆	☆
Variables	☆	☆	☆	☆	☆	☆	☆	☆	☆
Data sources/ Measurement	☆	☆	☆	☆	☆	☆	☆	☆	☆
Bias							☆		
Study size	☆	☆	☆	☆	☆		☆	☆	☆
Quantitative variables	☆	☆	☆	☆	☆	☆	☆	☆	☆
Statistical methods		☆	☆	☆	☆	☆	☆	☆	☆
Results									
Participants	☆	☆	☆	☆	☆	☆	☆	☆	☆
Descriptive data	☆	☆	☆	☆	☆	☆	☆	☆	☆
Outcome data	☆	☆	☆	☆	☆	☆	☆	☆	☆
Main results	☆	☆	☆	☆	☆	☆	☆	☆	☆
Other analyses	☆	☆	☆	☆	☆	☆	☆	☆	☆
Discussion									
Key results	☆	☆	☆	☆	☆	☆	☆	☆	☆
Limitations		☆		☆	☆	☆	☆	☆	☆
Interpretation	☆	☆	☆	☆	☆	☆	☆	☆	☆
Generalizability	☆	☆	☆	☆	☆	☆	☆	☆	
Funding information	☆	☆	☆		☆	☆	☆	☆	☆

3. Results

3.1. Study selection

From our electronic search, we identified a total of 356 studies (Fig. 1). We found an additional 3 records by hand searching from the reference lists of other review articles. Of these, 323 studies were remained after removing the duplicates. Two hundred and 72 irrelevant records were excluded by screening the titles and abstracts. Of the remaining 51 papers, 30 articles were excluded due to letters, reviews, and meta-analysis. Twenty-one studies were evaluated in detail and of these, 12 studies were excluded, 7 are without control and 5 presented unusable data. Finally, 9 observational studies[24–31] with 8901 participants according to the inclusion criteria were included in our study.

3.2. Characteristics of the studies

Nine studies assessed 8901 participants, including 2308 athletes and 6593 controls. Study characteristics are summarized in Table 1. The included studies were published between 1998 and 2015. The number of participants per study ranged from 124 to 3993. The mean age of the patients in each study varied between 39 and 72.8. Methodological quality of observational studies included in the meta-analysis was shown in Table 2. In the 9 observational studies, 8 studies presented statistical methods, 7 studies adequately described their study limitations in the discussion, and 8 presented their funding sources.

3.3. Quantitative synthesis

Overall, the risk of AF was significantly higher in the athletes group than in controls (OR=2.34, 95% CI=1.04 to 5.28, $P_{heterogeneity}$ <.001, I^2=92.3%, Fig. 2).

3.4. Evaluation of heterogeneity

Subgroup analysis based on gender demonstrated a significantly increased risk in men (OR=4.03, 95% CI=1.73 to 9.42, $P_{heterogeneity}$ <.001, I^2=82.7%, Fig. 3A). Based on the mean age, significant result was obtained for the mean age group of <60 (OR=3.24, 95% CI=1.23–8.55, $P_{heterogeneity}$ <.001, I^2= 84.3%, Fig. 3B). In the subgroup analysis based on study type, a significant risk was found in the case–control group (OR=5.10, 95% CI=3.07–8.46, $P_{heterogeneity}$=.343, I^2=10%, Fig. 3C). Based on the sample sizes, the group with sample sizes <300 demonstrated significant results (OR=4.91, 95% CI=3.08–7.84, $P_{heterogeneity}$=.341, I^2=10.4%, Fig. 3D). In the subgroup analysis based on sports mode, a significantly increased risk was found in the group with single type (OR=3.97, 95% CI=1.16–13.62, $P_{heterogeneity}$=.018, I^2=70.4%, Fig. 3E). There was heterogeneity among studies in overall comparisons and also subgroup analyses. To explore the sources of heterogeneity across studies, we assessed mean age and sample size by logistic meta-regression analysis. Meta-regression analyses revealed that age (P=.131, Fig. 4A) did not explain the heterogeneity across studies, but sample size (P=.044, Fig. 4B) was partly associated with heterogeneity among the studies.

3.5. Sensitive analysis

Sensitivity analyses were performed to assess the influence of individual study on the pooled ORs by sequential removing each eligible study. As seen in Figure 5, omission of any single study showed no change in the overall statistical significance, indicating that our results are statistically robust.

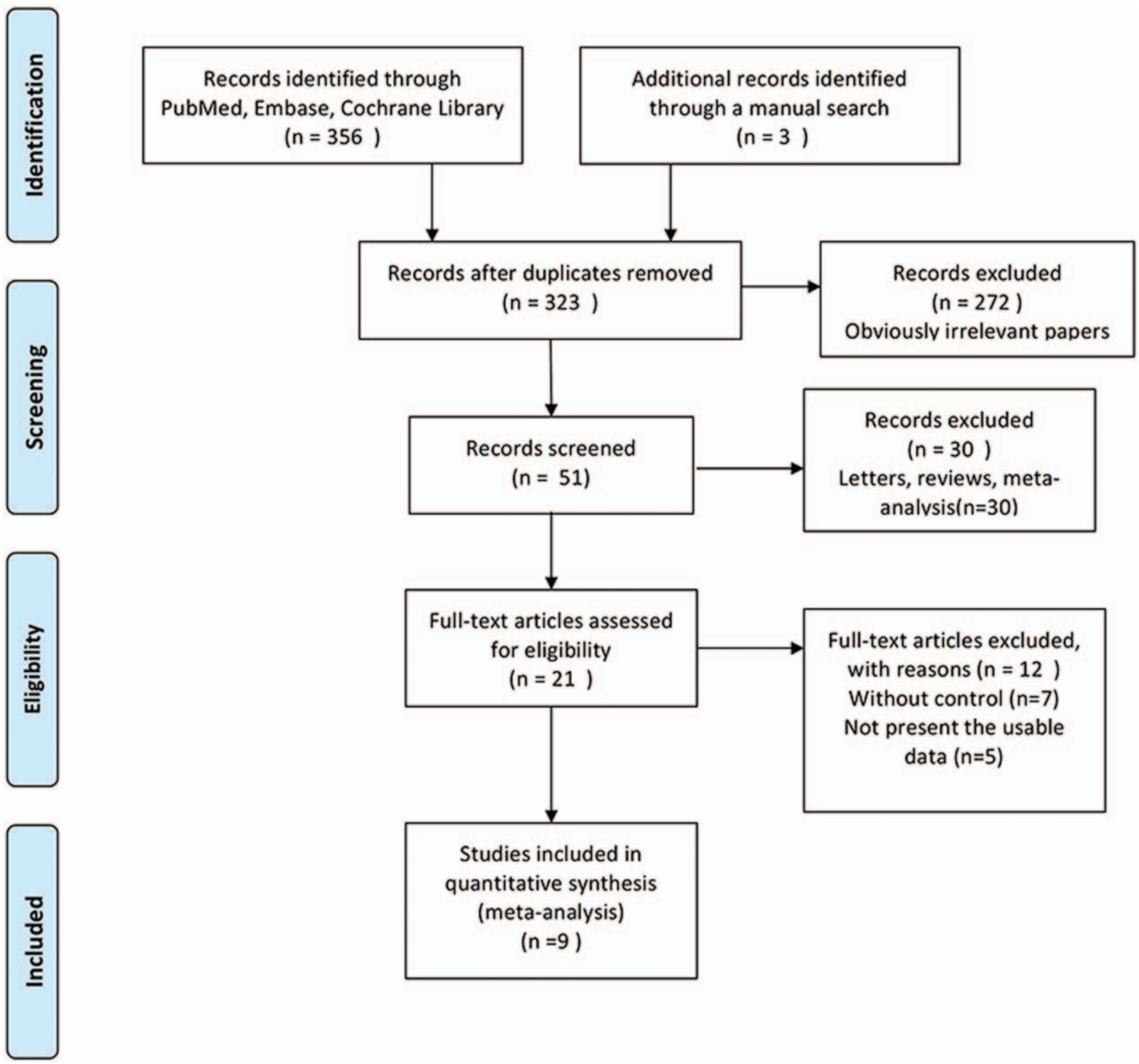

Figure 1. Flow diagram of studies identification.

3.6. Publication bias

Begg funnel plot and Egger test were performed to assess publication bias among the literature. As shown in Figure 6, there was no evidence of publication bias (Begg test $P = .754$; Egger test $P = .144$).

4. Discussion

To the best of our knowledge, this is the largest study reported so far that analyzed data from 9 trials with 8901 participants and evaluated whether the risk of AF was higher in athletes compared to general population. Our results showed that the risk of AF was significantly higher in athletes than in general population. A consideration is that the average age of our study population ranged from 39 to 72.8 years, where the age range was larger compared to the studies that demonstrated an increased AF risk with exercise. One study that reported an increased risk of lone AF with vigorous exercise also demonstrated that the increased risk disappeared among participants >50 years of age.[16] Subgroup analysis based on mean age showed significant result only for the Mean age group of <60 in this systematic review and meta-analysis. Furthermore, a recent study[17] demonstrated that in patients >75 years, AF was more likely to be asymptomatic. Early studies of athletes with arrhythmias showed that most athletes were young, male, and competitive in the elite level.[32,33] About 25 percent of these arrhythmias were AF. Some case–control studies examined lone AF patients clinically[25,34] or in emergency department.[28] In these studies, ORs of AF in patients who performed vigorous exercise ranged from 3.13 to 15.11. Again, most of the patients were male. This systematic review and meta-analysis have included general population and athletes, and have examined both men and women, with mean age ranging between 39 and 72.8 years old.

The risk of AF in athletes and general population has been investigated by previous meta-analysis studies. Recently, Abdulla et al[35] conducted a systematic review and meta-analysis about the risk of AF in athletes and non-athletes. Results demonstrated that the risk of AF was significantly higher in athletes compared

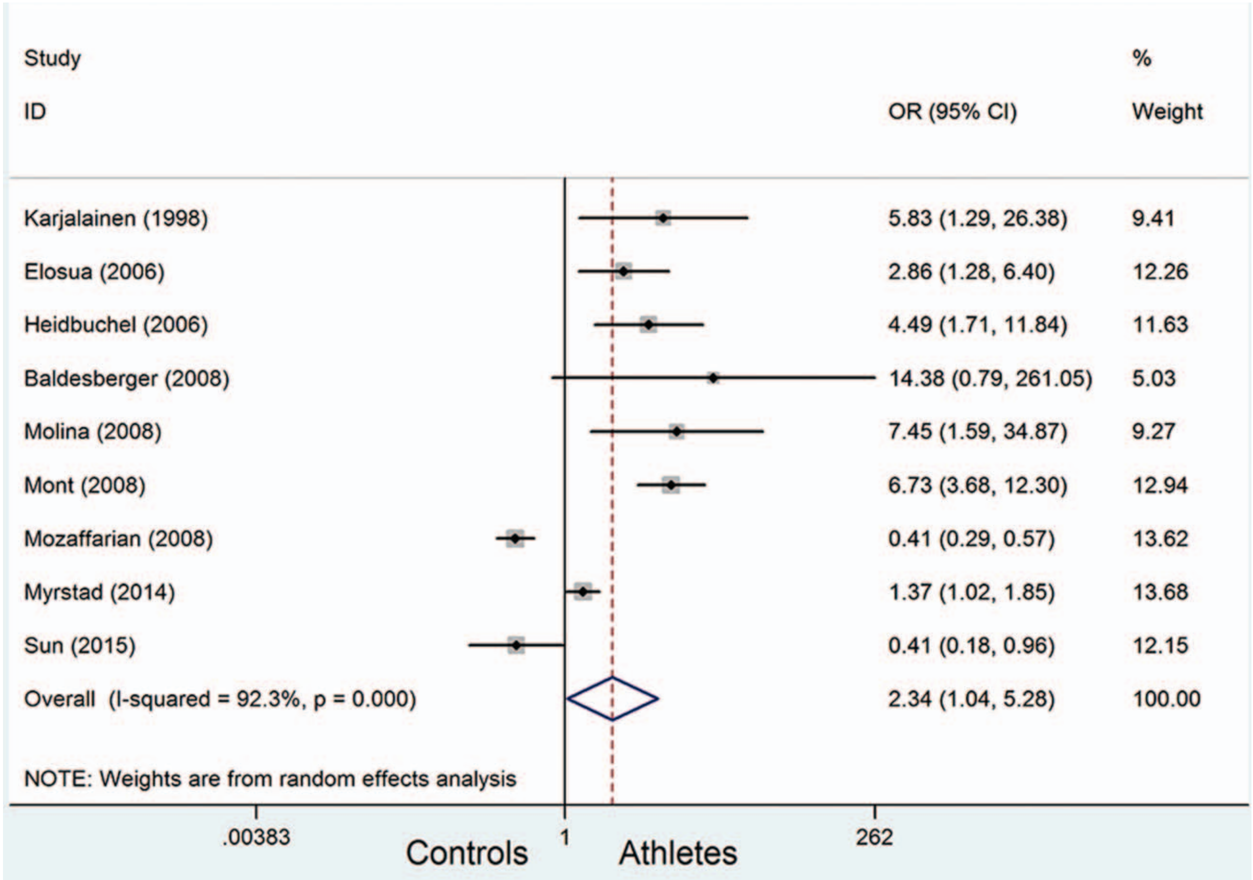

Figure 2. Risk of incident AF in athletes compared with general population. AF=atrial fibrillation.

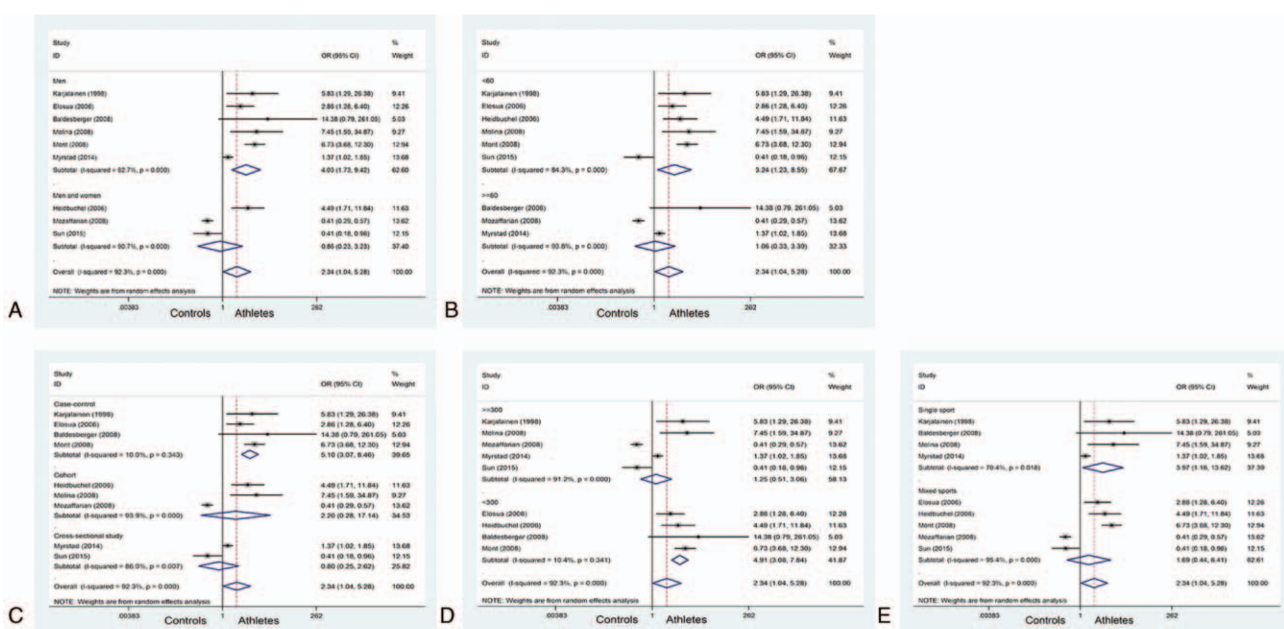

Figure 3. Subgroup analysis of risk of incident AF in athletes compared with general population. A) Gender; B) Mean age; C) Study design; D)Sample size; E) Sports mode. AF=atrial fibrillation.

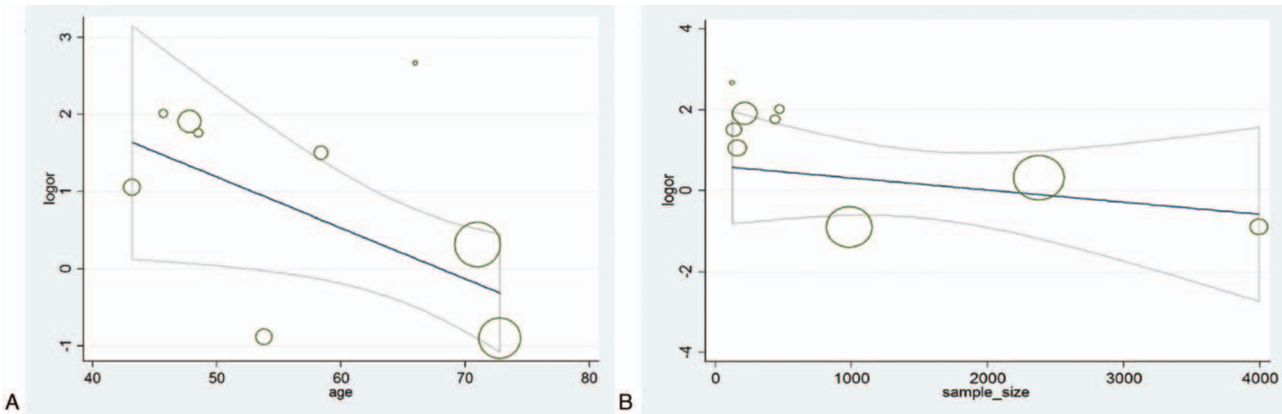

Figure 4. The logistic meta-regression analysis for exploring sources of heterogeneity. A) Mean age; B) Sample size.

to non-athletes. These results are entirely consistent with our study findings. Compared with Abdulla's work, we identified more eligible studies[29–31] and performed a detailed subgroup analysis. The study carried out by Abdulla et al consisted of only 6 studies with a total of 695 cases and 895 controls, while our study analyzed data from 9 studies with 2308 athletes and 6593 non-athletes. Our study population included not only men but also women. Furthermore, our systematic review and meta-analysis demonstrated that the risk of AF was significantly higher in athletes compared with general population, especially in male athletes <60 years old.

Heterogeneity is a potential problem when interpreting the results of meta-analyses. In this meta-analysis, heterogeneity was found in overall comparison and subgroup analyses, and thus, the random-effects model was used. The "sample size" partly explained the heterogeneity across studies by logistic meta-regression analyses. There may be other reasons accounting for the heterogeneity in the risk of AF. Nevertheless, sensitivity analysis proved that our meta-analysis results were statistically reliable.

5. Limitations

First, the included studies in the athletic populations were of small size and not randomized controlled in nature. Second, the studies demonstrated significant heterogeneity. To explore the sources of heterogeneity across studies, we did stratified and logistic meta-regression analyses. The heterogeneity might be partially due to the differences in gender, mean age, and sample size. Third, few studies had AF determined by self-reported questionnaires, which might lead to an underestimation of the events.

5.1. Future directions

Future well-designed large studies are necessary to clarify the risk of AF in athletes compared with general population.

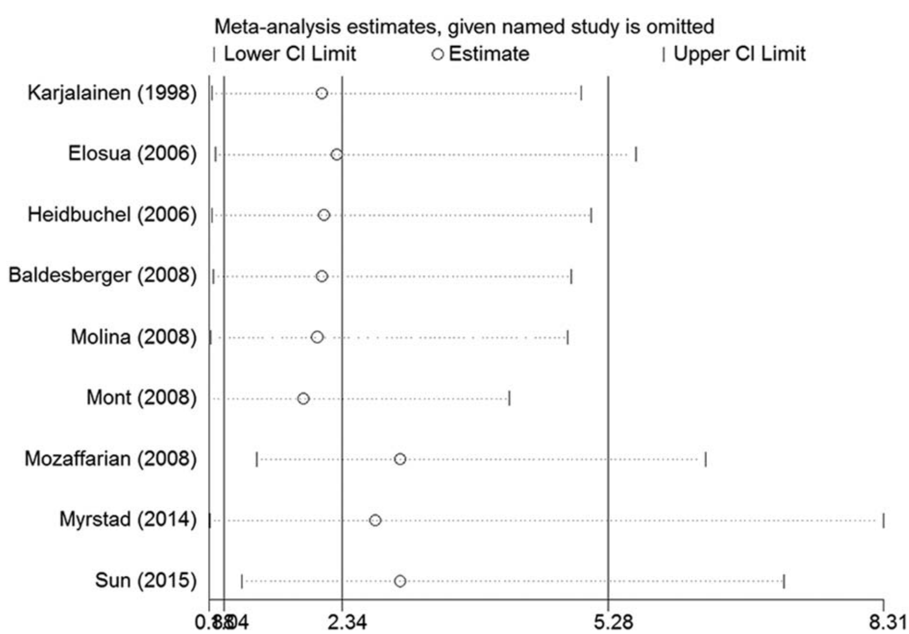

Figure 5. Sensitivity analysis of risk of incident AF in athletes compared with general population. AF = atrial fibrillation.

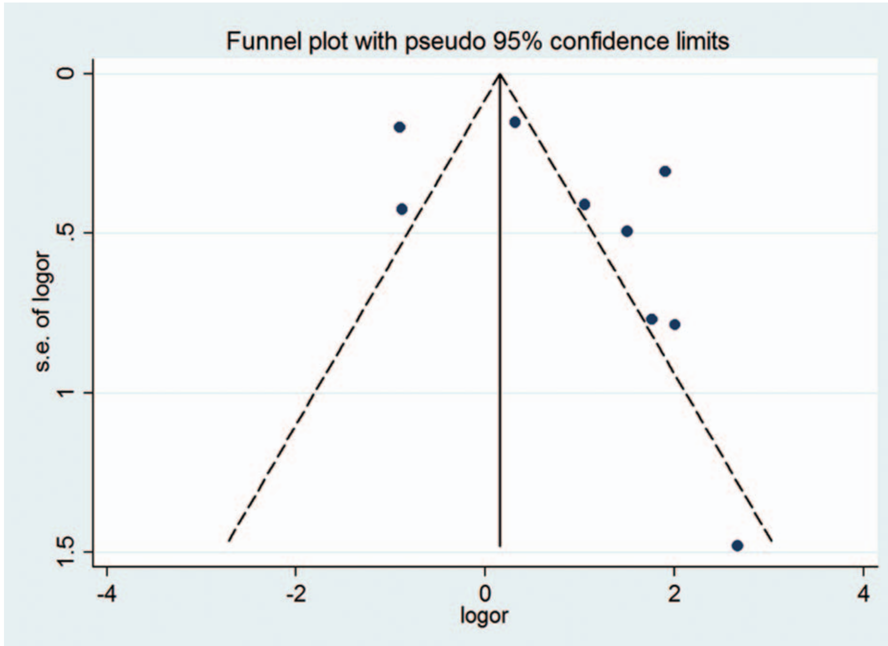

Figure 6. Funnel plot for publication bias test. Each point represents a separate study for the indicated association.

6. Conclusion

In summary, our results demonstrated that the risk of AF was significantly higher in athletes than in general population, especially among men aged <60.

Author contributions

Conceptualization: Xiangdan Li.
Data curation: Songbiao Cui, Dongyuan Xu.
Formal analysis: Xiangdan Li, Chunhua Xuan.
Funding acquisition: Xiangdan Li, Songbiao Cui.
Investigation: Dongchun Xuan, Dongyuan Xu.
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Software: Xiangdan Li, Dongchun Xuan.
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Validation: Dongyuan Xu.
Visualization: Songbiao Cui, Dongchun Xuan, Chunhua Xuan.
Writing – original draft: Xiangdan Li, Songbiao Cui.
Writing – review & editing: Xiangdan Li, Dongyuan Xu.

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